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(54) Title: PROSTHETIC DEVICES

(57) Abstract

Prostheses, e.g. disc nucleus prostheses comprising a resiliently deformable material are reinforced with physically discrete structures to form a composite. The resiliently deformable material may be a hydrophilic polymer such as a hydrogel.

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PROSTHETIC DEVICES

The present invention relates to prosthetic devices and in particular to such devices which deform when in use (e.g. when under compressive load).

One type of prosthesis is disclosed in US Patent No. 5047055 and comprises a hydrogel material in a shape which generally conforms to the intervertebral disc nucleus pulposes. When hydrated the hydrogel comprises a certain amount of free water which can leave the prosthesis when the disc is partially dehydrated or under mechanical pressure.

Another type of intervertebral disc nucleus prosthesis is disclosed in US Patent No. 5192326. The prosthesis comprises a multiplicity of hydrogel beads. The beads are covered by an external, semi-permeable membrane, which functions to retain the beads, but which permits fluids to flow in and out of the prosthetic nucleus.

The hydrogel materials employed in these prior devices have a tendency to become weaker and less able to withstand compressive loading as they become more fully hydrated. This may lead to failure of the prosthesis by fragmentation of the prosthesis material.

The present invention seeks to reduce the risk of stress failure of said prostheses to reduce the risk of fragmentation which may lead to adverse reactions in a host.

According to the present invention there is provided a prosthesis comprising a composite of a synthetic resiliently

deformable material having at least partially embedded therein a physically discrete reinforcing structure.

In addition to ameliorating disadvantages with prior art devices a further advantage of the prosthesis of the present invention is that it allows a wider range of resiliently deformable materials to be utilised than was hitherto the case. This is because the reinforcing structure can substantially contribute to the physical strength of the device, thereby allowing weaker deformable materials to be used than is the case with non reinforced prostheses.

The prosthesis of the present invention is suitable for replacing body components which are subject to repeated and variable compressive loads and may be shaped so as to correspond to suitable body components. For example it may be used to replace the nucleus pulposus of the intervertebral disc, the intervertebral disc in its entirety, as a replacement for the articular cartilage in joints, in place of orthopaedic bearing surfaces (eg to replace polyethylene bearing surfaces), in total joint replacement implants such as the hip, knee, shoulder, wrist, ankle, fingers and toes, as a spacer to replace segments of bone or the bone in its entirety, as a space filling implant replacing soft tissue for orthopaedic, maxillo-facial, or plastic or reconstructive surgical applications - such as to replace or augment deficiencies in bone, cartilage or soft tissue.

Preferably however the prosthesis is adapted to replace part or all of an intervertebral disc of a mammal, e.g. a human, and is shaped accordingly. Most preferably the prosthesis is adapted to replace an intervertebral disc nucleus and it therefore desirably has

a shape generally corresponding to that of a natural disc nucleus. Alternatively it may comprise a plurality of sections which are adapted, when fitted together to approximate the shape of the natural disc nucleus. For example, the nucleus may be in two halves to allow easy manipulation and to facilitate minimally invasive surgical techniques.

The reinforcing structure can be located partially or totally within the resiliently deformable material and is formed of a material which is physically discrete from said resiliently deformable material (although the reinforcing structure may itself be resiliently deformable). It is thus distinguished from systems in which polymers forming the resiliently deformable material are simply cross-linked. The material comprising the reinforcing structure may also be chemically distinct from that of the resilient material.

The reinforcing structure may function by providing a restraining means within the deformable material which reduces the tendency of the latter to shear or otherwise fail when under compressive load.

Desirably, the resiliently deformable material is in solid or semi-solid form. It may be an elastomeric polymer. Preferably it is hydrogel or a hydrophilic polymer.

Suitable hydrogels include PVA hydrogels, such as those disclosed in US-A-5192326.

Other suitable materials for the production of hydrogels or hydrophilic polymers include:

1. Acrylates:- eg acrylic acid, methacrylic acid, 2-hydroxyethyl

methacrylate, and copolymers thereof with N-vinyl pyrrolidone, N-vinyl lactams, acylamide, polyurethanes, polyacrylonitrile; copolymers of N-vinyl pyrrolidone and glycidyl acrylate, copolymers of polyethylene, polytetrafluoroethylene or polypropylene with acrylic acid, block copolymers of poly (2-hydroxyethyl methacrylate) with polystyrene, or poly (dimethyl-siloxane), para-hydroxyperfluoro-alkyl styrene, or trifluoroethyl methacrylate;

2. Acrylamides:- eg acrylamide, methacrylamide and copolymers of acrylamides such as polyacrylamide-agarose gels, siloxy-acrylamides;

3. Silicones:- eg 1,3-bis-methacryloxy-propyl-1,1,3,3-tetrakis (trimethyl-siloxy) disiloxane, tris (trimethyl-siloxy) silyl-propyl methacrylate, siloxane monomers, polysiloxane-polyoxyalkylene macromers, silicone rubbers, hexamethyl disiloxane, triethoxyvinyl silane, hexamethyl disilazane;

4. Collagen:- eg copolymers with poly (2-hydroxyethyl-acrylate) or poly (vinyl alcohol);

5. Vinyl compounds:- eg N-vinyl pyrrolidone, N-vinyl lactams, hydroxyethyl cellulose vinyl and vinylic monomer, polymers of vinyl carbonate or vinyl carbamate, vinyl trifluro acetate;

6. Polyurethanes:- eg polyether, or short chain polyester based polyurethanes.

7. Naturally occurring materials (or chemically modified variants thereof):- eg glucomannan gel, hyaluronic acid, proteins, polysaccharides or polypeptides combined with a polymer of a

hydrophilic acrylic or methacrylic acid derivative, crosslinked carboxyl containing polysaccharides, carboxymethyl cellulose, gelatin, alginates.

Preferred hydrogels have a water content of at least 30% (w/w) when fully hydrated at 37°C, more preferably of from 75 to 99%(w/w).

Other elastomeric polymers which may be suitable for use in the present invention include:- silicone and fluorosilicone elastomers, phosphazene elastomers, vinylidine fluoride based fluoroelastomers, natural and artificial rubbers, etc.

The prosthesis of the invention aptly has a compressive strength of at least 1MNm^{-2} at 37°C and at atmospheric pressure.

Suitable reinforcing structures include:- nets; foams; knitted, braided, crocheted, woven, or non-woven fabrics; arrays of spaced reinforcing elements; particulate filler materials; loose fibres.

The term "net" includes perforate films as well as fibrous networks. Suitable nets include those formed of nylon™. dacron™, carbon fibre etc.

The foams may be open cell foams, closed cell foams, skeletal foams, non-skeletal foams, etc. Foams which are already used in wound-dressings for example those polyurethane foams employed in wound dressings such as ALLEVYN™ foam, which is sold by Smith & Nephew Medical Ltd, Hull, UK may be particularly suitable.

The fabrics used for reinforcing structures are aptly arranged as composite structures having desirably first and second spaced apart sheets whose opposed surfaces are maintained in a spaced apart relationship by a plurality of supporting members. The first and second spaced apart surfaces may be generally parallel to one another (when the fabric is not compressed). They may be generally planar or may present corrugated surfaces. Such fabrics are often formed by warp knitting using Raschel warp knitting machinery (as described eg in USPN 4601940 and EP-A-0529671). Certain type of fabrics of this are sometimes referred to as "spacer fabric" and have been used in seating in the automotive industry. Such fabrics can be obtained from Messrs. Nippon Mayer Co. Ltd. of J-910 Fukui City, Japan; Müller Textile GmbH of D-51674 Wiehl-Drabenderhöhe, Germany; or Karl Mayer Textilmaschienen fabrik of D-63160 Obertshaüsen, Germany.

The surfaces of these composite structures may be maintained in the spaced apart relationship by, for example, columns of elastomeric material or by a plurality of fibrous members arranged, for example to form a web. Such webs may be formed from non-woven fabrics.

The particulate filler material may employed is the reinforcing structure may be quartz, silica, gypsum, titanium dioxide, glass based fillers, clay-based fillers, or calcium carbonate. Filler materials are described in detail in the "Handbook of Fillers for Plastics" by Katz and Mikwski [1987], published by Van Nostrand Reinhold.

In certain cases the resiliently deformable material may be contained within an outer cover, which is desirably flexible.

Aptly the outer cover is suitably non-permeable to body fluids.

Alternatively, the outer cover may be provided to simply serve to assist in maintaining integrity or strength of the prosthesis. The outer cover may therefore be permeable to body fluids but prevent the resiliently deformable material and the reinforcing structure from passing through it. Aptly such outer covers will be in the form of a membrane or mesh. Various outer covers are disclosed in US-A-5192326.

In the case of a replacement intervertebral disc, it may be desired to provide a prosthesis with additional means to externally reinforce and/or anchor the device.

This may take the form of a collar surrounding the prosthesis to constrain its lateral deflection. This collar may be of metal, polymeric, ceramic or composite construction and would surround the prosthesis circumferentially. This collar may be made of implantable metals such as stainless steel, cobalt chrome alloy, titanium alloy or ceramic materials such as alumina or zirconia, or composite materials such as carbon fibre reinforced PEEK, or polymers such as polyethylene. Alternatively the prosthesis may be bonded to plates of metal, ceramic, polymer or composite construction which are interspersed between the prosthesis and the bone of the vertebral bodies in cephalad and caudad directions to facilitate anchorage to the bone.

Once the prosthesis of the present invention has been formed it is necessary to introduce it into a host. This can be done by any appropriate surgical technique, but minimally invasive techniques are preferred where possible.

In order to introduce a prosthesis consisting of an inter-vertebral disc nucleus prosthesis into the human body this may be done from the dorsal direction by dissecting away skin, soft tissue and muscle exposing the dorsal aspect of the spinal column. A laminectomy or other surgical procedure may be performed to remove the dorsal bony elements from the column to expose the disc. The disc nucleus prosthesis is then placed in position through a surgical defect created in the posterior surface of the annulus fibrosis.

Alternatively the spinal column may be approached from the dorsal-lateral direction without removing the dorsal bony elements, again introducing the disc nucleus prosthesis through a defect created surgically in the annulus fibrosis. As a further alternative, an ventral approach to the spinal column may be used entering the body through the peritoneum or thorax to expose the ventral surface of the spinal column. The disc nucleus prosthesis would then be introduced through a defect created surgically in the anterior surface of the annulus fibrosis.

In each of these cases it is anticipated that the effected disc level would be distracted using standard surgical instruments to increase the height of the damaged disc to allow insertion of the disc nucleus prosthesis. Any of these surgical approaches may be made using a minimally invasive surgery technique such as arthroscopy, endoscopy or laparoscopy to approach the spinal column. In this case the disc nucleus prosthesis would be introduced through a defect created surgically in the annulus fibrosis through a cannula using a percutaneous approach.

The prosthesis may be dehydrated to reduce the volume of the prosthesis prior to insertion. The disc would then either be rehydrated in situ after implantation or be permitted to absorb water from the surrounding tissues during the post-operative period. This technique is particularly suitable for hydrogel prostheses.

A complete intervertebral disc prosthesis could be introduced into the human body using any of the techniques described above, with the modification that the entire disc annulus fibrosis and nucleus pulposus or a substantial portion thereof would be removed using standard surgical procedures exposing the vertebral bones, cephalad and caudad to the disc space, and the prosthesis inserted to replace the entire disc. A prosthesis could be anchored using any of the means described previously.

The following examples, which are not to be construed as limiting, illustrate ways in which articles can be formed from resiliently deformable material and reinforced with reinforcing structures. For convenience the examples illustrate the production of generally cylindrical articles. In practice however these techniques would be used to produce a prosthesis, or a component thereof, shaped as desired.

Example 1 - Synthesis of polyurethane structures reinforced with nets

The following reagents were stirred together at 60°C until a homogenous composition was obtained:-

86.3g of ethanediol

565.7g of freshly dried polyethylene glycol PEG 1500

447.9g of Desmodur W (Trade Mark for a 4,4 - Dicyclohexylmethane di-isocyanate (obtainable from Bayer UK Limited).

2.2g of Metatin 812ES catalyst (Trade Mark for a dioctyltin dilaurate catalyst obtainable from Cima Chemical Industries) was then added with vigorous stirring until exotherm commenced, after which the mixture was poured onto a polypropylene tray then covered with PTFE sheet and placed in an oven to cure at 90°C for 2 hours to produce a hydrophilic polyurethane, which is referred to herein as "HPU 45"

The cured HPU 45 was then broken into small pieces and dissolved by adding 15 parts by weight of tetrahydrofuran to 85 parts by weight of HPU 45.

The resultant liquid was poured into shallow trays and left to evaporate solvent slowly in a fume cupboard over 19 hours. The samples were dried in an oven at 40°C for 4 hours then in a vacuum oven at 40°C for 3 hours. The resultant films were removed from the trays, turned over and the trays replaced in the vacuum oven for a final 5.5 hours.

Equally sized discs of diameter 14mm and thickness 1mm were then cut out of the films. From a polyalkylene net obtainable from Smith & Nephew Extruded Films Ltd. of Gilberdyke, UK under the designation of "Net 909 (Grade L40)" further discs of diameter 14mm were cut. The thickness of these discs was 0.15mm and the nets weighed 13.6 g/m^2.

Different arrangements were produced as follows:-

Sample A - Stack consists of two HPU 45 discs, then one net disc, then two HPU 45 discs, then one net disc, then two HPU 45 discs.

Sample B (control) - Stack consists of six HPU 45 discs.

Once the stacks were formed the discs were laminated together by heating in an oven at 100°C for 10 mins with a 15g weight being placed on the top of each stack.

After removal from the oven, the laminated stacks were allowed to cool to room temperature.

Example 2 - Synthesis of a poly Hydroxyethylmethacrylate hydrogel reinforced with a knitted fabric.

A stock solution was prepared by adding azoisobutylnitrile to hydroxyethylmethacrylate (HEMA) at a level of 0.15% w/w. The solution was then de-aerated by bubbling with nitrogen for 15 mins.

A mould was obtained for producing moulded discs shaped articles of diameter 14mm and depth 9mm. The solution was powered into the mould to a depth of about 2mm and a disc cut out of a knitted "spacer fabric" to have a diameter of 14mm was placed above the HEMA (once it had thickened sufficiently to support the disc). The knitted fabric was obtainable from under the designation of Karl Meyer Textelmaschinen Fabrik of D.63160 Obertshausen, Germany and consists of two planer surfaces interconnected by monofilaments. Each planar surface is knitted to provide a "honeycomb" structure of interconnecting hexagons. It has a thickness of about 5mm.

The solution was then poured over the knitted fabric a until the mould was full and the mould was then sealed and put in a water bath (containing a tablespoon of sodium metabisulphite) at 50°C for 3 hours. The temperature was then increased to 80°C for 2 hours and then reduced to 60°C for 17 hours. The mould was finally put in an oven at 100°C for 24 hours to anneal.

After cooling at room temperature for several hours the mould was opened and the moulded article, referred to as sample C, was removed.

A control sample, sample D, was also prepared, using a corresponding procedure to that described above except that no knitted fabric was used (ie sample D consisted of poly HEMA only).

A further control sample, sample E, was prepared, consisting of a sample of the knitted fabric only, cut to the same size as the moulded samples.

Physical Testing of Samples

Static compression testing was carried out on samples prepared according to Examples 1 and 2 using a Rheometrics Solid Analyser RSA II, available from Rheometrics (UK), Englefield Green, Surrey, UK. In the tests strain was increased in steps of 0.2% up to approximately 30%.

The testing was carried out on hydrated samples, hydration being performed by immersing samples in 0.9% w/v saline solution

at 37°C until no further net intake of water occurred (as determined by weighing samples after various time periods).

Complete stress-strain curves are shown in Fig. 1 for hydrated samples A and B (as indicated by the corresponding letters). In some cases more than one of each type of sample was prepared and therefore more than one stress-strain curve is shown.

The results are variable and most samples showed an initially low gradient which increases with increasing load. This is probably due to the fact that some samples were uneven and the top and bottom surfaces were not perfectly parallel.

In Fig. 2 the upper parts of the stress-strain curves are shown and it can be seen that at higher loads the traces become more linear. Because of the variability of the initial parts of the curves due to the uneven samples, compression modulus values were obtained by taking the gradient of the curves at higher loads (between 20-30 kPa) and then were found to give more reproducible results. Moduli calculated from Fig. 2 are summarised in Table 1.

Table 1

Hydrated Sample	Modulus/kPa	Mean Modulus/kPa
B	236	234
	233	
A	280	
	280	284
	293	

The results show an average increase of over 20% in stiffness for the samples with 2 layers of net compared to samples with
HPU45 alone.

The same testing procedure described above was performed upon samples C, D and E and the results are shown in Figs. 3 and 4. Gradients were calculated at high loads (20-30 kPa) and the results are illustrated in Table 2 below.

Table 2

Sample	Modulus/kPa	Mean Modulus/kPa
D	644	643
	625	
	660	
C	923	863
	855	
E	424	424

The results show an average increase in stiffness of over 30% for the poly HEMA samples reinforced with the knitted fabrics relative to poly HEMA alone.

CLAIMS

1. A prosthesis comprising a composite of a synthetic resiliently deformable matrix material having at least partially embedded therein a physically discrete reinforcing structure.

2. A prosthesis as claimed in claim 1 having a compression strength of at least $1MNm^{-2}$ (at 37°C and atmospheric pressure).

3. A prosthesis as claimed in claim 1 or claim 2 wherein the resiliently deformable material is a hydrophilic polymer.

4. A prosthesis as claimed in claim 3 where the hydrophilic polymer is a hydrogel.

5. A prosthesis as claimed in claim 4 wherein the hydrogel has a water content of at least 30% (w/w) when fully hydrated at 37°C.

6. A prosthesis as claimed in any one of the preceding claims wherein the reinforcing structure comprises one or more materials chemically distinct from that of the resiliently deformable material.

7. A prosthesis as claimed in any one of the preceding claims wherein the reinforcing structure comprises a net, a foam, knitted, woven or non-woven fabrics.

8. A prosthesis as claimed in claim 7 wherein the reinforcing structure comprise at least one pair of sheets maintained in spaced apart relationship by a plurality of supporting members.

9. A prosthesis as claimed in claim 8 wherein the supporting members are physically defined by fibrous web.

10. A prosthesis as claimed in any one of the preceding claims wherein the resiliently deformable material is at least partially enveloped by and contained within a cover.

11. A prosthesis as claimed in claim 10 wherein the cover is non-permeable to body fluids.

12. A prosthesis as claimed in claim 10 or claim 11 wherein the cover forms part of the reinforcing structure.

13. A prosthesis as claimed in claim 10 or claim 11 wherein said sheets as defined in claim 8 comprise the cover.

14. A prosthesis as claimed in any one of the preceding claims further provided with additional wholly external support means.

15. A disc nucleus prosthesis as defined in any one of the preceding claims.

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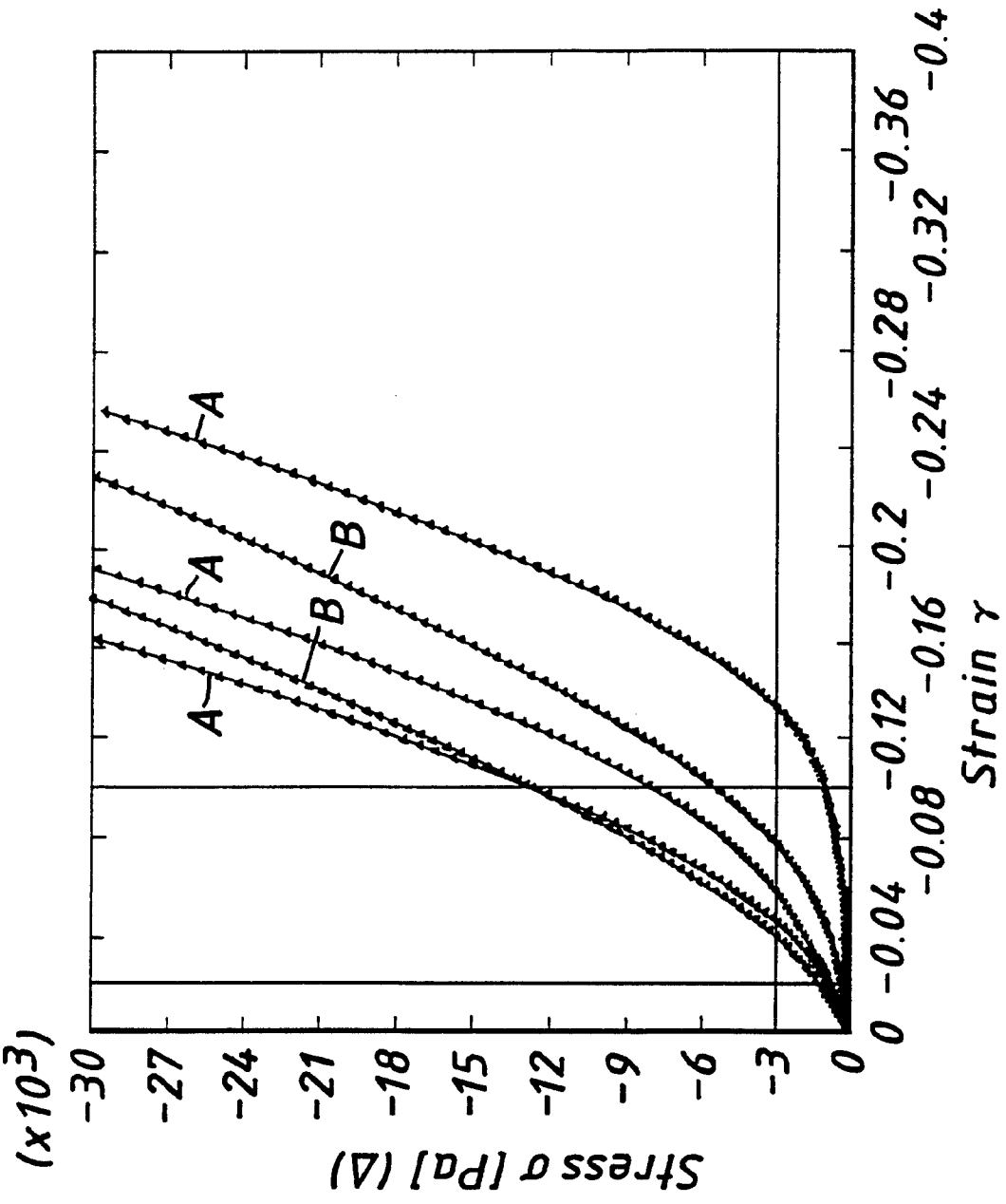
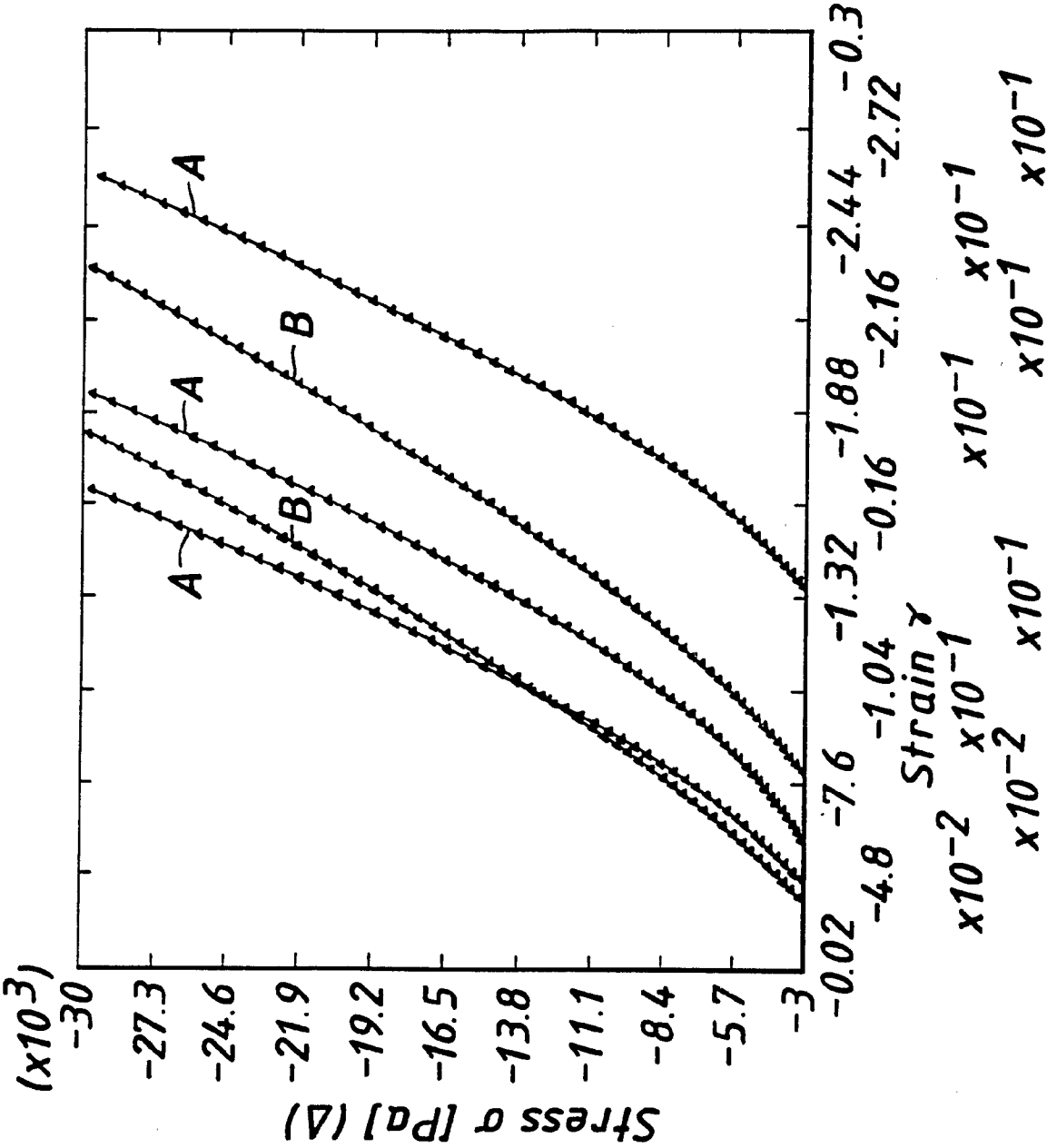

Stress σ [Pa] (Δ)
(x10^3)
-30
-27
-24
-21
-18
-15
-12
-9
-6
-3
0
Strain γ
0
-0.04
-0.08
-0.12
-0.16
-0.2
-0.24
-0.28
-0.32
-0.36
-0.4
A
B
A
B
A

FIG.1.


Stress σ [Pa] (Δ)
(x10^3)
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-27.3
-24.6
-21.9
-19.2
-16.5
-13.8
-11.1
-8.4
-5.7
-3
-0.02
-4.8
-7.6
-1.04
-1.32
-0.16
-1.88
-2.16
-2.44
-2.72
-0.3
Strain γ
x10^-2
x10^-1
A
B

FIG.2.

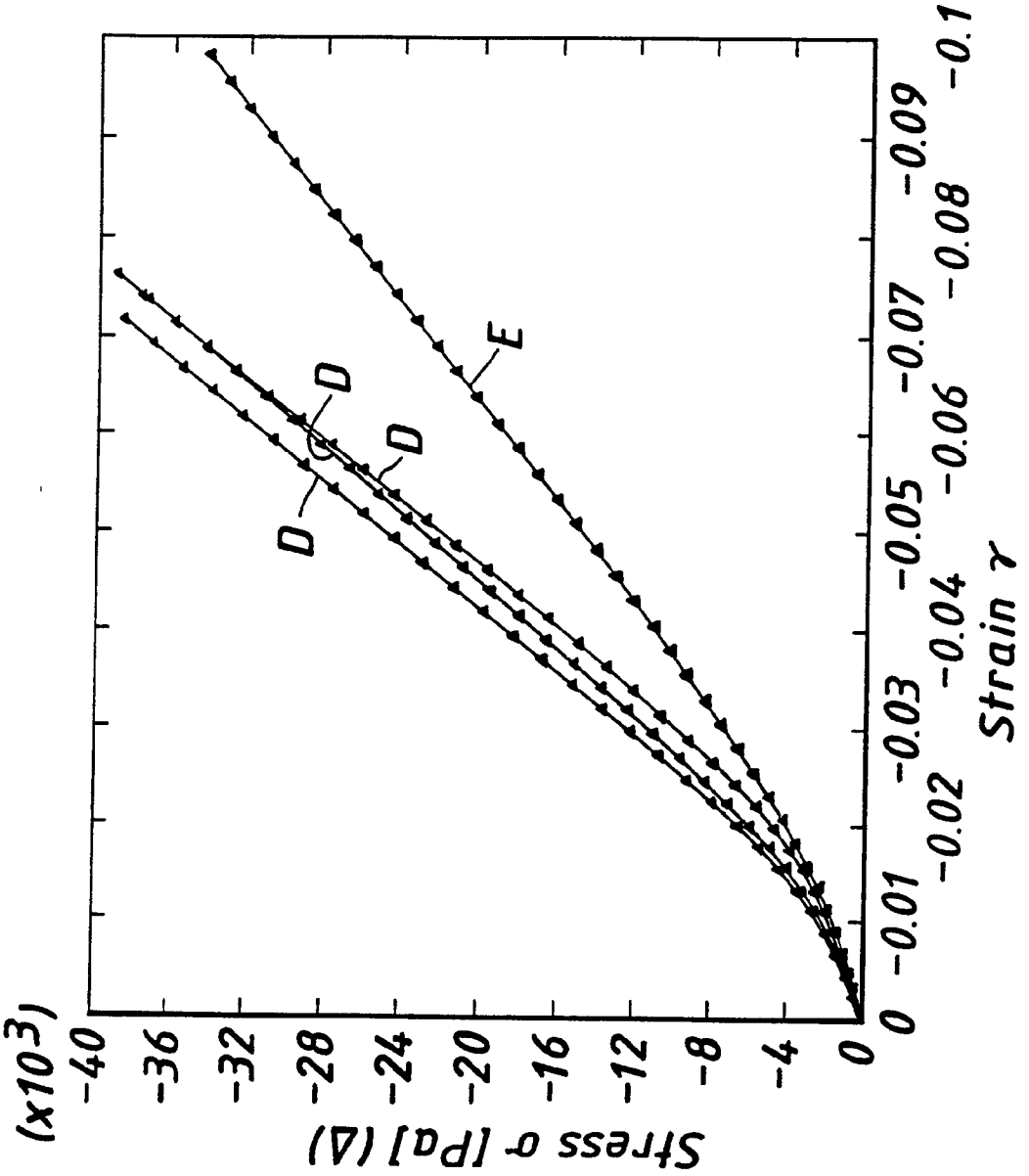
Stress σ [Pa] (Δ)
(x10^3)
-40
-36
-32
-28
-24
-20
-16
-12
-8
-4
0
Strain γ
0
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.1
D
D
D
E

FIG. 3.

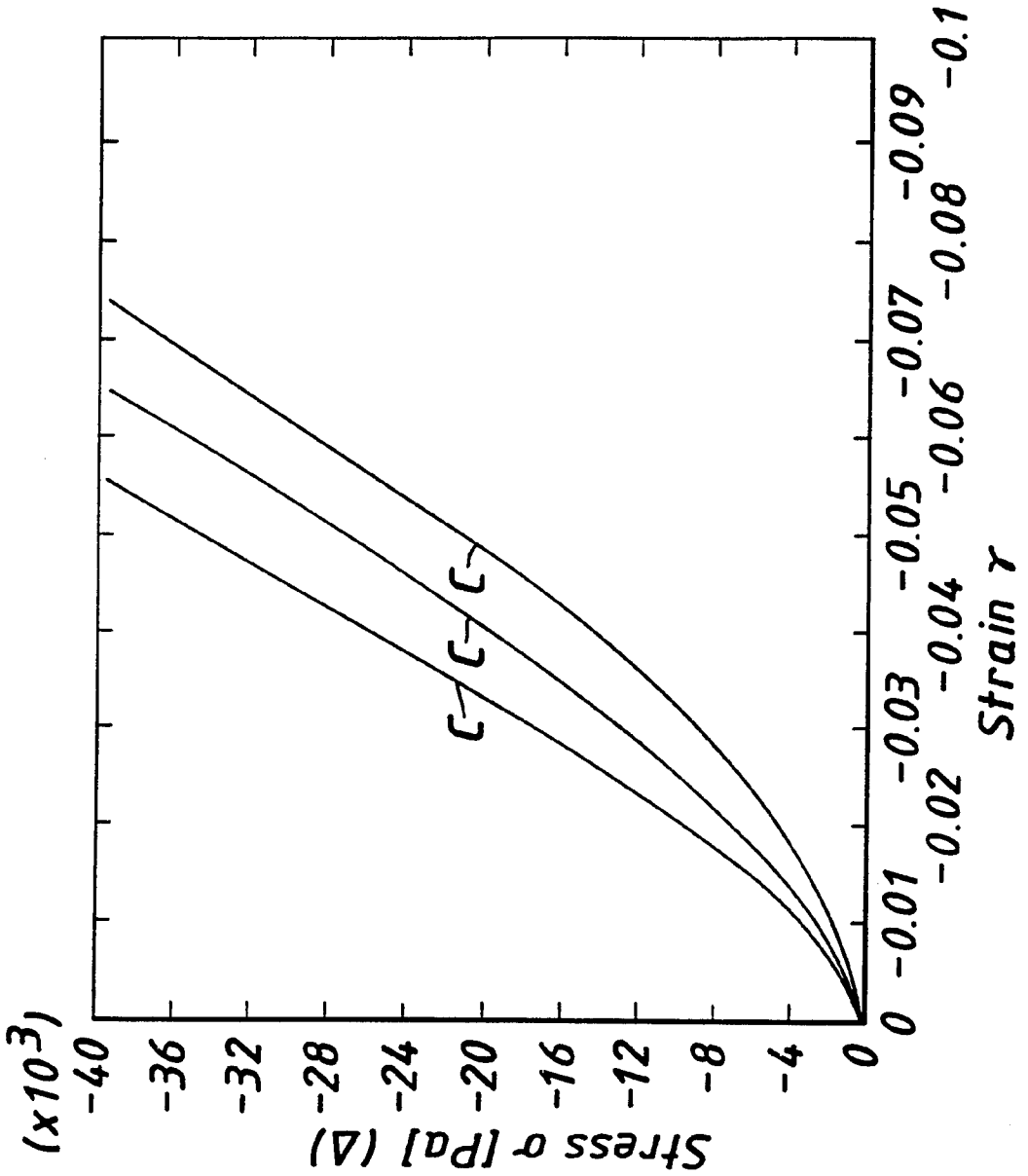
Stress σ [Pa] (Δ)
(x10^3)
-40
-36
-32
-28
-24
-20
-16
-12
-8
-4
0
0
-0.01
-0.02
-0.03
-0.04
-0.05
-0.06
-0.07
-0.08
-0.09
-0.1
Strain γ

FIG. 4.

INTERNATIONAL SEARCH REPORT

Int. onal Application No
PCT/GB 95/01550

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61F2/02 A61F2/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US,A,3 867 728 (CUTTER LABORATORIES, INC.) 25 February 1975 see column 10, line 41-54; figures	1,2,6-15 3-5
Y	US,A,5 047 055 (PFIZER HOSPITAL PRODUCTS GROUP, INC) 10 September 1991 cited in the application see the whole document	3-5
A	EP,A,0 346 129 (JOHNSON & JOHNSON) 13 December 1989	
A	EP,A,0 372 811 (STRYKER CORPORATION) 13 June 1990	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
3 October 1995	13.10.95

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Steenbakker, J

Form PCT/ISA/210 (second sheet) (July 1992)

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PCT/GB 95/01550

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		GR-A-	89100383	11-05-90
		JP-A-	2224659	06-09-90
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		CA-A-	2003991	02-06-90
		JP-A-	2195955	02-08-90